IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Juan Colberg, et al.	**Examiner:**	Mark L. Berch
Serial No.:	10/781,158	**Art Unit:**	1624
Filed:	February 17, 2004	**Docket No.**	PC10856B

For: PROCESS AND ESTER DERIVATIVES USEFUL FOR PREPARATION OF CEPHALOSPORINS

Confirmation No.:
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22314-1450

DECLARATION UNDER 37 C.F.R. §1.132

Sir:

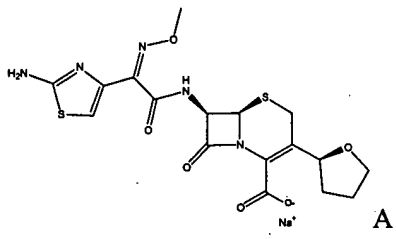
I, JUAN C. COLBERG, declare and state as follows:

1. I received a PhD degree in organic Chemistry from University of Puerto Rico, Rio Piedras Campus, San Juan Puerto Rico, in 1994. Attached as Exhibit A is a copy of my Curriculum Vitae which indicates some of the reports and papers I have published, the awards I have won, and my employment history;

2. from 1993 to present I have been and continue to be employed at Pfizer Inc., the assignee of the above-identified application;

3. I am a co-inventor in the above-referenced patent application;

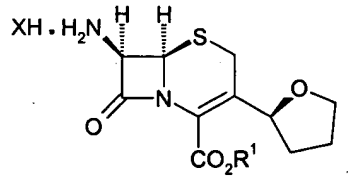
4. I was a member of a team which investigated the development of a commercial process for the synthesis of a long-acting cephalosporin of formula **A**, which is known under the generic name cefovecin, and which is described in US Patent No. 6,001,997;



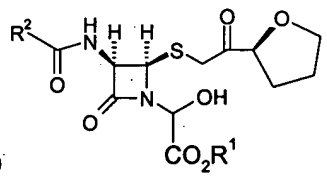
A

5. my group, in developing a commercial process for producing cefovecin and its intermediates, studied the process of Bateson, set forth in US Patent No. 6,001,997;

6. the processes set forth in Bateson for the preparation of intermediates of cefovecin of formulae **I** and **IIIc**



(I)



(IIIc)

where CO_2R^1 is an ester derivative, $R^2C(O)$ is an acyl group and X is halo, were deemed inadequate for commercialisation compared to the processes my group developed, as established by the claims of the above-identified application;

7. to substantiate the superiority of the processes defined by the claims of the present application, the processes disclosed by Bateson were compared to the claimed processes of the above-identified application in experiments conducted by me or under my supervision;

8. for the synthesis of a compound of formula **I**, utilizing the Bateson process, an ester compound of formula **IIIc**, where R^1 is *para*-methoxybenzyl and R^2 is phenyl, was converted to a compound of formula **I**, where R^1 is *para*-methoxybenzyl and X is chloro, using the four step process set out in Example 1 of the above-identified application;

9. the form and purity of the resulting compound of formula **I** from the reaction was unacceptable for further use due to an unacceptable high level of impurities. The crude product required purification by column chromatography and the compound of formula I was obtained in an overall yield of 22% as a yellow foam. The yield was defined as the mass of the compound of formula **I** obtained as a percentage of the theoretical yield of the compound of formula **I** for the four step process;

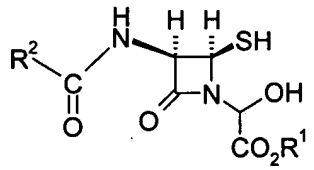
10. the Bateson process was compared with the process of present claim 1 wherein the compound of formula **IIIc**, where R^1 is *para*-nitrobenzyl and R^2 is

phenyl, to produce a compound of formula **I**, where R^1 is *para*-nitrobenzyl and X is chloro;

11. the compound of formula **I** obtained by the practice of the process of claim 1 of the present application was in a crystalline solid form of sufficiently high purity so that no purification operations were necessary prior to further use. The compound of formula **I** was obtained in a yield of 45%, where yield is again defined as the mass of the compound of formula **I** obtained as a percentage of the theoretical yield of the compound of formula **I** for the four step process;

12. the above results establish the clear superiority of the present process of claim 1 over the Bateson process. That the compound having the formula **I** was produced and isolated in acceptable purity and with higher yields, as set forth in Example 1 of the specification of the present application, and that it was very useful in the synthesis of cefovecin, was surprising;

13. for synthesis of a compound of formula **IIIc**, further utilising the Bateson process, an ester compound of formula **V**



(V)

where R^1 is *para*-methoxybenzyl and R^2 is phenyl, was converted to a compound of formula **IIIc**, by treatment with 2-bromo-1-(tetrahydro-furan-2-yl)-ethanone, under the process set out in Example 5 of the above-identified application, where the compound of formula **V** is generated *in situ*;

14. the form and purity of the compound of formula **IIIc** resulting from the reaction was unacceptable for further use due to an unacceptable high level of impurities. The crude product required purification by column chromatography and the compound of formula I was obtained in an overall yield of 55% as a white foam, where the yield is again defined as the mass of the compound of formula **IIIc** obtained as a percentage of the theoretical yield of the compound of formula **IIIc** for the process;

15. the Bateson process for preparation of a compound of formula **IIIc** was compared with the process of claim 10 in the present application for the compound of formula **V**, where R^1 is *para*-nitrobenzyl and R^2 is phenyl, to produce a compound of formula **IIIc**, where R^1 is *para*-nitrobenzyl and R^2 is phenyl;

16. the compound of formula **IIIc** obtained by the practice of the process of claim 10 was in a solid form of sufficiently high purity so that no purification operations were necessary prior to further use. The compound of formula **IIIc** was obtained in a yield of 86%, where yield is again defined as the mass of the compound of formula **IIIc** obtained as a percentage of the theoretical yield of the compound of formula **IIIc** for the process;

17. the above results establish the clear superiority of the present process of claim 10 over the Bateson process. That the compound having the formula **IIIc** was produced and isolated in acceptable form and with higher yields, as set forth in Example 5 of the specification of the present application, and that it was very useful in the synthesis of cefovecin, was surprising; and

18. that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that wilful false statements and the like so made are punishable by fine, imprisonment, or both, under section 1001 of title 18 of the United States code and such wilful false statements may jeopardize the validity of the application or any patent issuing thereon;

Further declarant sayeth not.

June 17, 2008

Date

Juan C. Colberg

Exhibit A

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EDUCATION

1994	Ph.D. in Chemistry, Major in Organic Dissertation: "From Olefins and Vinylsilanes to Non-Steroidal Antiinflamatory Agents via B-Alkenyl-9-BBN Derivatives" University of Puerto Rico, Rio Piedras Campus, San Juan Puerto Rico

EXPERIENCE

2004-present	Pfizer Global Research & Development Groton,Connecticut Associate Director
2003-2004	Pfizer Global Research & Development Groton,Connecticut Associate Research Fellow
2000-2003	Pfizer Global Research & Development Groton,Connecticut Senior Research Investigator
1999-2000	Pfizer Central Research Groton, Connecticut Senior Research Scientist
1997-1999	Pfizer Pharmaceutical Groton, Connecticut Development Scientist
1993-1997	Pfizer Pharmaceutical Inc. Barceloneta, Puerto Rico
1995	Senior Process Development Chemist Project Leader
1994	Senior Process Development Chemist
1993	Process Development Chemist
1991-1993	Interamerican University, Metropolitan Campus Rio Piedras, Puerto Rico Organic and Analytical Chemistry Assistance Professor
Awards	EPA's 2002 Presidential Green Chemistry Award for "Green Chemistry in the Re-Design of the Setraline Process."

PUBLICATIONS

1. ***The Hydroboration for Silylacetylene: Silyl Markovnikov Hydroboration. Route to Pure Z-1-(2-borylsilane) and B-Ketosilane."***

   Soderquist, J.A.; Colberg, J.C.; Del Valle, L. *J.Am.Chem.Soc.* **1989**, *111*, 4873.

2. ***Stereodefined ß,ß-disubstituted vinylsilanes from the silicon-diverted Hydrogenation of alkynylsilances and palladium chemistry.***

   Soderquist, J.A.; Colberg, J.C. *Synlett* **1989**, 1, 25.

3. ***Ibuprofen and Naproxen via Organoboranes.***

   Soderquist, J.A.; Colberg, J.C.; Rivera, I. *Tetrahedron Lett.* **1992**, *33*, 6915.

4. ***Trans-vinylboranes from 9-Borabicyclo[3.3.1.]nonane through Dehydroborylation.***

   Soderquist, J.A.; Colberg, J.C.; Rane, A.; Vaquer, J. *J.Am. Chem. Soc.* **1993**, *115,* 6065.

5. ***Trans-vinylsilanes via Suzuki-Miyaura Coupling.***

   Soderquist, J.A.; Colberg, J.C.; *Tetrahedron Lett.* **1994**, *35*, 6915.

6. ***Pure Trans-vinylboranes via Dehydroborylation.***

   Soderquist, J.A.; Colberg, J.C.; Rane, A.; Vaquer, J. *Current Topics in the Chemistry of Boron, Royal Society of Chemistry,* UK, **1994**, pp 72-77.

7. ***Trans-3-Silyl allylic alcoholsvia the Brown vinylation***

   Soderquist, J.A.; Colberg, J.C.; Rane, A.; Vaquer, J. *Tetrahedron Lett.* **1995**, *36*, 987.

8. ***Cyclization of a,w-Diborylalkanes via Double Suzuki-Miyaura Coupling.***

   Soderquist, J.A.; Colberg, J.C.; Leon, G.; Martinez, I. *TETRAHEDRON LETT.* **1995**, 35, 3119.

9. ***Novel Process for Preparing a Ketimine.***

   Colberg, J.C.; Pfisterer, D.; Taber, G.P.
   PCT Int. Appl. 24 pp. CODEN: PIXXD2 WO 9936394 A1 990722
   CAN 131:116073; AN 1999:464268.